CLAIMS

We claim:

5

10

15

A method of treating hemophilia in a human comprising:

- a) providing at least one recombinant adeno-associated virion comprising nucleotide sequences encoding Factor VIII; and
- b) administering said at least one recombinant adeno-associated virion into said human under conditions such that said Factor VIII nucleotide sequences are expressed at a level which provides a therapeutically effective amount in said human.

2. The method of Claim 1, wherein said Factor VIII nucleotide sequences are expressed in the liver of said human.

- 3. The method of Claim 1, wherein said recombinant adeno-associated virion encodes the light chain of said Factor VIII.
 - 4. The method of Claim 1, wherein said recombinant adeno-associated virion encodes the heavy chain of said Factor VIII.
- 5. The method of Claim 1, wherein said adeno-associated virion is administered intravenously.
 - 6. The method of Claim 1, wherein the nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.

25

COL

- 7. A method of treating a subject comprising:
 - a) providing:
 - i) a subject suffering from a blood clotting disorder,
 - ii) a first recombinant adeno-associated virion, comprising a nucleotide sequence encoding the light chain of Factor VIII, and
 - iii) a second recombinant adeno-associated virion comprising a nucleotide sequence encoding the heavy chain of Factor VIII; and
 - b) administering said first and second recombinant adeno-associated virions into said subject under conditions such that said Factor VIII heavy and light chain nucleotide sequences are expressed at a level which provides a therapeutic effect in said subject.
- 8. The method of Claim 7, wherein said recombinant adeno-associated virion is administered intravenously.
- 9. The method of Claim 7, the nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.

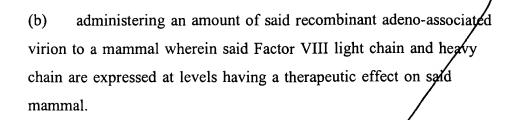
10

10

- 10. A method of treating hemophilia in a mammal comprising:

 (a) providing
 - i) a recombinant adeno-associated virion, wherein said recombinant adeno-associated virion comprises a nucleic acid encoding Factor VIII operably linked to an expression control element, and
 - ii) a mammal; and
- (b) administering an amount of said recombinant adeno-associated virion to a mammal wherein said Factor VIII is expressed at levels having a therapeutic effect on said mammal.
- 11. The method of Claim 10 wherein said nucleic acid encodes the light and heavy chains of Factor VIII.
 - 12. The method of Claim 10, wherein said mammal is a human.
- 13. The method of Claim 10, wherein said administering comprises introducing said recombinant adeno-associated virion to the liver of said mammal.
- 14. The method of Claim 10, wherein said recombinant adeno-associated virion is introduced intravenously.
 - 15. The method of Claim 14, wherein the recombinant adeno-associated virion is introduced via the portal vein.
- 25 16. The method of <u>Claim 10</u>, wherein said recombinant adeno-associated virion is introduced arterially.

- 17. The method of Claim 16, wherein said recombinant adeno-associated virion is introduced via the hepatic artery.
- 18. The method of Claim 10, wherein said nucleic acid comprises SEQ ID 5 NO: 13.
 - 19. The method of Claim 10, wherein said nucleic acid comprises SEQ ID NO: 14.
- 10 20. The method of Claim 10, wherein said expression control element is tissue-specific.
 - 21. The method of Claim 10, wherein the expression control element is liver-specific.
 - 22. The method of Claim 10, said nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.
 - 23. A method of treating/hemophilia A in a mammal comprising:
 - (a) providing:
 - i) a recombinant adeno-associated virion wherein said recombinant adeno-associated virion comprises a nucleic acid encoding a Factor VIII lacking a portion of the B-domain region and wherein said nucleic acid is operably linked to an expression control element, and
 - ii) a mammal suffering from hemophilia A; and



- 24. The method of Claim 23, wherein said nucleic acid encodes the light and heavy chains of Factor VIII.
 - 25. The method of Claim 23, wherein said mammal is a human.

10

15

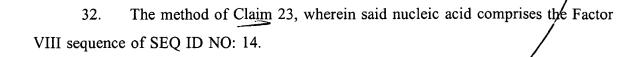
- 26. The method of Claim 23, wherein said administering step comprises introducing the recombinant adeno-associated upon to the liver of said mammal.
- 27. The method of Claim 23, wherein said recombinant adeno-associated virion is introduced intravenously.
 - 28. The method of Claim 27, wherein said recombinant adeno-associated virion is introduced via the portal vein.

20

- 29. The method of Claim 23, wherein said recombinant adeno-associated virion is introduced arterially.
- 30. The method of Claim 29, wherein said recombinant adeno-associated is introduced via the hepatic artery.

25

31. The method of Claim 23, wherein said nucleic acid comprises the Factor VIII sequence of SEQ ID NO: 13.



- 33. The method of Claim 23, wherein said expression control element is tissue-specific.
 - 34. The method of Claim 23, wherein the expression control element is liver-specific.
- The method of Claim 34, wherein said Factor VIII nucleotide sequences are expressed in the liver of said subject.
 - 36. The method of Claim 23, wherein said nucleotide sequences are operably linked to tissue-specific expression control elements.
 - 37. The method of Claim 23, wherein said nucleotide sequences are operably linked to liver-specific expression control elements.
- 38. The method of Claim 23, wherein said Factor VIII nucleotide sequences are operably linked to a tissue-specific expression control element.
 - 39. The method of Claim 38, wherein said Factor VIII nucleotide sequences are operably linked to a liver-specific expression control element.
- 25 40. The method of Claim 23, said nucleic acid encodes the amino acid sequence set forth in SEQ ID NO:15.